

AMENDMENTS TO THE CLAIMS

1. (previously presented): A method for modifying a nucleotide sequence that encodes a functional first modular polyketide synthase (PKS) so as to alter the nature of an extender unit employed by said first PKS which method consists of:

excising by restriction enzyme reaction a region of said nucleotide sequence encoding an acyltransferase (AT) domain of said first PKS-encoding nucleotide sequence and ligating into said first nucleotide sequence a second AT-domain-encoding region of a second PKS-encoding nucleotide sequence that has been excised by restriction enzyme reaction,

wherein the extender unit specificity of said first region is different from the extender unit specificity of the second region, and wherein the modular PKS from which the first region is excised is not the modular PKS from which the second region is obtained,

to produce a modified nucleotide sequence encoding a functional PKS which uses a different extender unit substrate from the unmodified form of the first PKS.

2. (original): The method of claim 1 wherein the first or second PKS is from *Saccharopolyspora erythraea*.

3. (original): The method of claim 1 wherein the first or second PKS is from *Streptomyces*.

4. (original): The method of claim 3 wherein the *Streptomyces* is *Streptomyces hygroscopicus*.

5. (original): The method of claim 1 wherein the first PKS or second PKS is selected from the group consisting of erythromycin, rapamycin, avermectin, FK-506, and tylosin.

6. (canceled)

7. (currently amended): A method for modifying the nature of the extender unit substrate used by a first modular PKS encoded by a first nucleotide sequence comprising a first AT domain-encoding region which method comprises:

effecting *in vivo* recombination, wherein said recombination is from a donor plasmid comprising [[said]] a second nucleotide sequence which is a second AT domain-encoding region of a second PKS-encoding nucleotide sequence framed by a first pair of flanking sequences,

into a recipient plasmid comprising said first nucleotide sequence encoding said first PKS wherein in said recipient plasmid a first AT domain-encoding region in said first PKS encoding nucleotide sequence is framed by a second pair of flanking sequences which are homologous to said first pair of flanking sequences,

wherein the extender unit specificity of said first region is different from the extender unit specificity of the second region

to produce a nucleotide sequence encoding a modified first PKS which uses a different extender unit substrate from the unmodified first PKS,

wherein said donor and recipient plasmids comprise different selectable markers, and wherein said donor plasmid is temperature sensitive.

8-9. (canceled)

10. (original): The method of claim 7 wherein the first or second PKS is from *Saccharopolyspora erythraea*.

11. (original): The method of claim 7 wherein the first or second PKS is from *Streptomyces*.

12. (original): The method of claim 11 wherein the *Streptomyces* is *Streptomyces hygroscopicus*.

13. (original): The method of claim 7 wherein the first PKS or second PKS is selected from the group consisting of erythromycin, rapamycin, avermectin, FK-506, and tylosin.

14-30. (canceled)

31. (previously presented): The method of claim 1 wherein at least one restriction site acted on by at least one restriction enzyme is inserted by PCR amplification.